

AMENDMENTS TO THE CLAIMS

Claim 1 (Previously Presented): A method for producing
N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester,
comprising:

(1) subjecting N-L- α -aspartyl-L-phenylalanine 1-methyl ester and
3-(3-methoxy-4-hydroxyphenyl)propionaldehyde or a derivative thereof to reductive alkylation
in a solvent to obtain
N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester;
and (2) crystallizing said
N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester,
wherein said reductive alkylation comprises catalytic hydrogenation, and
wherein said derivative thereof is selected from the group consisting of
3-(3-methoxy-4-hydroxyphenyl)-2-propenylaldehyde,
3-(3-methoxy-4-protected-hydroxyphenyl)propionaldehyde,
3-(3-methoxy-4-protected-hydroxyphenyl)-2-propenylaldehyde, and
acetals derived therefrom.

Claim 2 (Previously Presented): The method of Claim 1, wherein said crystallizing said
N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester
comprises any one of the following crystallization methods:

- a. crystallization with a solvent useful for crystallization;
- b. crystallization after extraction with water; and
- c. crystallization after separation of N-L- α -aspartyl-L-phenylalanine 1-methyl ester.

Claim 3 (Canceled)

Claim 4 (Previously Presented): The method of Claim 1, wherein said solvent for said reductive alkylation reaction is at least one solvent selected from the group consisting of alcohols, tetrahydrofuran, acetonitrile, toluene, acetic acid, acetic acid esters, and mixed solvents which comprise at least one of these organic solvents and water.

Claim 5 (Previously Presented): The method of Claim 2, wherein said N-[N-[3-(3-methoxy-4-hydroxyphenyl) propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester is crystallized by a process of concentration or by a process for solvent substitution.

Claim 6 (Previously Presented): The method of Claim 1, wherein said solvent for said crystallization of said N-[N-[3-(3-methoxy-4-hydroxyphenyl) propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester is at least one solvent selected from the group consisting of alcohols, tetrahydrofuran, acetonitrile, toluene, ether, acetone, acetic acid, acetic acid esters, and mixed solvents which comprise at least one of these organic solvents and water.

Claim 7 (Previously Presented): The method of Claim 1, wherein said solvent for said crystallization of said N-[N-[3-(3-methoxy-4-hydroxyphenyl) propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester is the same solvent which has been used in the reductive alkylation reaction.

Claim 8 (Previously Presented): The method of Claim 5, wherein said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester is crystallized by solvent substitution using at least one solvent selected from the group consisting of alcohols, tetrahydrofuran, acetonitrile, toluene, ether, acetone, acetic acid, acetic acid esters, and mixed solvents which comprise at least one of these organic solvents and water.

Claim 9 (Previously Presented): The method of Claim 1, wherein said solvent of said reductive alkylation reaction is one or more alcohols or a mixed solvent of one or more alcohols and water, and the solvent of said crystallization of said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester is one or more alcohols or a mixed solvent comprising one or more alcohols.

Claim 10 (Currently Amended): The method of Claim 2, wherein said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester is crystallized after extraction with water using at least one solvent selected from the group consisting of alcohols, tetrahydrofuran, acetonitrile, toluene, ether, acetone, acetic acid, acetic acid esters, and mixed solvents which comprise at least one of these organic solvents and water.

Claim 11 (Previously Presented): The method of Claim 2, wherein said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester is crystallized after extraction with water and said extraction with water is conducted with a mixed solvent which comprises water and one or more organic solvents, wherein said organic

solvent forms a layer which separates from an aqueous layer upon mixture with water, and said N-[N-[3-(3-methoxy-4-hydroxyphenyl) propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester is extracted into the aqueous layer.

Claim 12 (Previously Presented): The method of Claim 11, wherein said organic solvent is at least one solvent selected from the group consisting of acetic acid esters, ether, chloroform, dichloromethane, hexane, toluene, alcohols, tetrahydrofuran, acetone, acetonitrile and acetic acid.

Claim 13 (Previously Presented): The method of Claim 2, wherein said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester is crystallized after having separated N-L- α -aspartyl-L-phenylalanine 1-methyl ester and is crystallized from is at least one solvent selected from the group consisting of alcohols, tetrahydrofuran, acetonitrile, toluene, ether, acetone, acetic acid, acetic acid esters, and mixed solvents which comprise at least one of these organic solvents and water.

Claim 14 (Previously Presented): The method of Claim 2, wherein said process for separating N-L- α -aspartyl-L-phenylalanine 1-methyl ester is a process for separating N-L- α -aspartyl-L-phenylalanine 1-methyl ester by crystallization or precipitation with at least one solvent selected from the group consisting of acetic acid esters, ether, chloroform, dichloromethane, hexane, toluene, alcohols, tetrahydrofuran, acetone, acetonitrile, acetic acid and water.

Claim 15 (Previously Presented): The method of Claim 1, wherein said reductive alkylation reaction is conducted in at least one organic solvent which dissolves the starting materials or a mixed solvent of said organic solvents and water, and when an insoluble material is present in the reaction mixture obtained after said reductive alkylation reaction, said insoluble material is separated by filtration.

Claim 16 (Canceled)

Claim 17 (Previously Presented): The method of Claim 1, wherein said catalytic hydrogenation is conducted in the presence of at least one catalyst selected from the group consisting of palladium, platinum, and rhodium based catalysts.

Claim 18 (Previously Presented): The method of Claim 1, wherein said catalytic hydrogenation is conducted at a hydrogen pressure of 0.1 to 1 MPa.

Claim 19 (Previously Presented): The method of Claim 1, wherein said reductive alkylation reaction is conducted at a temperature range of from 15 to 50 °C, and a reaction time of from 2 to 48 hours.

Claim 20 (Previously Presented): The method of Claim 1, wherein said reductive alkylation reaction is carried out in a reaction solvent having a pH of from 4 to 6.5.

Claim 21 (Previously Presented): The method of Claim 1, wherein the molar ratio of said N-L- α -aspartyl-L-phenylalanine 1-methyl ester to said 3-(3-methoxy-4-hydroxyphenyl)propionaldehyde or derivative thereof ranges from 0.5 to 2.

Claims 22. – 28. (Canceled)

Claim 29 (Previously Presented): The method of Claim 1, wherein said 3-(3-methoxy-4-hydroxyphenyl) propionaldehyde or derivative thereof is prepared by subjecting 3-(3-methoxy-4-hydroxyphenyl)-2-propenylaldehyde or an acetal thereof, wherein the hydroxyl group may be protected, to reduction to obtain said 3-(3-methoxy-4-hydroxyphenyl) propionaldehyde or derivative thereof.

Claim 30 (Previously Presented): The method of Claim 29, wherein said reduction is conducted in the presence of a reduction catalyst or a rhodium based catalyst.

Claims 31. – 32. (Canceled):

Claim 33 (Previously Presented): The method of Claim 2, wherein said crystallization of said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester is carried out in the same a solvent which has been used in said reductive alkylation reaction.

Claim 34 (Canceled)

Claim 35 (Previously Presented): The method of Claim 2, wherein said solvent of the reductive alkylation reaction is one or more alcohols or a mixed solvent of one or more alcohols and water, and the solvent of the crystallization of said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester is one or more alcohols or a mixed solvent comprising one or more alcohols.

Claims 36. – 39. (Canceled)